

A Study of the Claisen Condensation.

DISSERTATION

SUBMITTED TO THE BOARD OF GRADUATE STUDIES OF
THE JOHNS HOPKINS UNIVERSITY IN CONFORMITY
WITH THE REQUIREMENTS FOR THE DEGREE
OF DOCTOR OF PHILOSOPHY.

BY

ERNEST E. GORSLINE.

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EASTON, PA. :
ESCHENBACH PRINTING COMPANY.
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A Study of the Claisen Condensation.

INTRODUCTION.

Very soon after the discovery of ethyl acetoacetate by Genther¹ a spirited discussion arose concerning its structure and the mechanism of the reactions involved in its formation.

Before any satisfactory conclusions were reached Claisen² discovered the reaction which has his name. As is well known, this reaction takes place between esters and ketones or aldehydes containing the groups —COCH_3 or $\text{—COCH}_2\text{R}$, in the presence of such agents as sodium or sodium ethylate. The synthesis of ethyl acetoacetate seems to be a special instance of the Claisen condensation.

Of the theories advanced concerning the mechanism of these reactions those of Claisen, A. Michael and J. U. Nef are now the most prominent.

While working with Claisen a method for the preparation of camphoroxalic acid was worked out by J. Bishop Tingle³ who condensed camphor and ethyloxalate by means of sodium wire, using petroleum ether as a solvent. This compound has been thoroughly studied by Tingle and his collaborators, and it seemed desirable to extend the study to other similar compounds.

Despite the large amount of discussion concerning the mechanism of the Claisen condensation, no systematic study had ever been made concerning the effects of temperature, or of a change in the solvent employed.

At the suggestion of Dr. Tingle, this investigation was undertaken, with the following objects in view: (a) To secure additional information concerning the effect of differ-

¹ Göttingen Anzeigen, 1768, p. 28.

² Ber. d. chem. Ges., 20, 646 (1887).

³ Inaug. Dis., Munich, 1889.

ent condensing agents. (b) To make a study of the effects of changes in temperature and solvent upon the reaction. (c) To work out a method by which compounds analogous to camphoroxalic acid can be obtained.

While studying the effects of various solvents, the fact that ether acts as a catalytic agent was observed. An investigation of this point has established a close analogy between the Grignard reaction and the Claisen condensation, so far as the effect of solvents is concerned, and seems to throw some additional light on the nature of these reactions.

After establishing the fact that ether and the tertiary bases act as catalytic agents in the Claisen condensation, a study of this reaction and of the acetoacetic ester synthesis was undertaken, in the hope of securing additional evidence concerning the disputed mechanism of the reactions.

The experimental results obtained cannot be reconciled with the view held by Claisen and Neff concerning the mechanism of the reaction, but seem to be in complete accord with the explanation advanced by A. Michael.

THEORETICAL.

The Effect on the Reaction of Varying Conditions.

A considerable number of experiments have been carried out for the purpose of determining the influence on the reaction and, therefore, on the yield of diketone of changes in the conditions. That such changes may exert a marked influence was shown some years ago by J. Bishop Tingle¹ in the case of camphoroxalic acid. The effect of variation of the temperature and of the solvent has been studied, and also the result of employing, as condensing agents, such substances as sodium, sodamide, and calcium. A few experiments with sodium ethylate free from alcohol and with sodium ethylate in absolute alcoholic solution have also been carried out. The last two reagents named have been used frequently by Claisen² and many other chemists, and the employment of metallic sodium is, of course, quite common.

¹ Am. Chem. J., 19, 393 (1897).

² Ber. d. chem. Ges., 38, 709.

A. *The Use of Calcium and Sodamide as Condensing Agents.*

—Camphor and the ethyl esters of oxalic, benzoic, and cinnamic acids have been condensed, using calcium and sodamide as the condensing agents. The temperature and solvent employed were also varied in each case. The results show that with camphor as the ketone, metallic calcium and sodamide are practically useless as condensing agents unless alcohol is added to the materials employed. Even then, the reaction must be carried out at a relatively high temperature. Under these conditions a fair yield may be obtained. This is quite different from the results recorded by Claisen,¹ who worked with sodamide, using acetone and acetophenone with ethyl acetate, and acetone with ethyl benzoate. It furnishes an illustration of the weighty influence exercised on the reaction by the nature of the ketone or aldehyde, and also by that of the ester.

Another matter of some importance and interest which this part of the work has demonstrated concerns the nature of the "solvent product" (*vide* p. 26). In the case of condensations between camphor and ethyl oxalate, in the presence of sodium, considerable quantities of camphoroxalic acid can be extracted from it.² The same is true when sodamide is used as the condensing agent, and also when this substance or sodium is brought into reaction with camphor and ethyl cinnamate. The results with calcium are in sharp contrast with this. In no single case has a trace of the condensation product been detected in the "solvent product." The difference may, of course, be due to the different solubilities of certain sodium or calcium compounds formed during the reaction.

B. *The Effect of Sodium Ethylate upon the Condensation.*—

The addition of a mere trace of alcohol, or of a solution of sodium ethylate in absolute alcohol, to the mixture of ketone, ester, sodium, and solvent starts a reaction very quickly, but the yield of the diketone is always greatly reduced. The important bearing of this fact upon one of the theories concerning the mechanism of the reaction will be discussed later.

¹ Ber. d. chem. Ges., **38**, 695 (1905).

² J. Bishop Tingle: Am. Chem. J., **19**, 393 (1897).

C. The Effect of Various Solvents and Temperatures.—

With the exception of J. Bishop Tingle,¹ who found that excellent yields of camphoroxalic acid could be obtained by the use of ligroin (b. p. 60°–70°), practically everybody who has utilized the Claisen condensation has either worked with solutions of anhydrous ether, free from alcohol, or has employed as the solvent an excess of the ester concerned in the condensation. Both of these methods were adopted by Claissen himself, who also described a few experiments with boiling toluene. These latter, however, gave extremely small quantities of the condensation compounds.

The solvents used in this work were ether, petroleum ether, (b. p. 36°), ligroin (b. p. 50°–55°) and (b. p. 70°–80°), hexane, (b. p. 90°), toluene and xylene.

As a rule the condensation proceeds more rapidly in ether than in any other solvent. In the case of some esters and ketones, however, the tendency to react is so great that variation in the solvent is without apparent effect on the velocity of the reaction or the yield of the diketone produced. It is found that, under otherwise similar conditions, the time and temperature factors are inversely proportional. The yield of the condensation product is practically the same in the two cases. Generally, however, other things being equal, better yields of diketones are obtained with higher- than with lower-boiling solvents; provided, of course, that the temperature is not sufficiently great to decompose the products of the reaction.

The question of the solvent action of ether and ligroin may now be taken up. Camphor and all of the esters which were employed dissolve in each solvent with great and, apparently, equal readiness, and the same is true of the condensation products; consequently the difference in solubility, if it exists, must be concerned with the sodium salts formed during the condensation of the ketone and ester. A good deal of attention has been paid to this point and it has been observed that the substances formed on the sodium wire sometimes flake off as rapidly as they are produced, and become partly

¹ *Loc. cit.*

suspended and partly dissolved in the solvent. Often there is a deposit of this material on the bottom of the flask. Frequently, however, it is all, or nearly all, in solution. Sometimes the sodium wire becomes thickly incrustated with a hard, rough coating of the salt, which clings to the metal and retains the general shape of the original wire. Contrary to expectations, the formation of this substance does not, in most cases, materially protect the sodium from being attacked by the reagents, nor does it adversely affect the yield of condensation product. Examination of the incrustated material will show that it often contains a minute thread of sodium.

The differences seem to depend upon extremely subtle changes in temperature, speed of reaction, etc., and it is impossible to define exactly the conditions necessary for obtaining any given result, though all of them will be observed if a considerable number of condensations is carried out. In some instances, moreover, the sodium salt formed remains incrustated over the wire and retains the wire form when examination shows that all of the sodium has disappeared. The interesting point in this connection is that the yield of condensation is essentially the same whether the sodium compound dissolves in the liquid, is suspended in it, or forms a crust over the sodium wire. In order to cast a little additional light on the subject a concentrated solution of sodium ethylate in alcohol was prepared. Equal volumes of ether, ligroin, benzene and toluene were mixed with separate, equal quantities of this alcoholic solution; in no case was a precipitate or a turbidity formed. As is well known, sodium ethylate free from alcohol is practically insoluble in ether or ligroin, but this fact has no direct bearing on these experiments.

D. The Influence of the Constitution of the Ester upon the Condensation.—On account of a delay in receiving a shipment of materials the work in this connection is much less complete than could be wished. The compounds employed may be classified as follows:

A. Aliphatic Series: Esters of formic, acetic, butyric, oxalic, malonic, and succinic acids.

B. Aromatic Series: Esters of benzoic, nitrobenzoic, cinnamic, and phthalic acids.

To obtain the condensation products when the above esters are allowed to react with camphor, it is generally necessary to extract with ether the acidified aqueous solution obtained by pouring the condensation product into ice water and removing the solvent layer. In a few cases the product will precipitate upon acidulation. Claisen¹ obtained oxymethylenecamphor in this way and the product of the ethyl phthalate-camphor condensation precipitates upon acidulation. By extracting with ether, every product, including the two above mentioned, is obtained in the form of a heavy, reddish brown oil. J Bishop Tingle² obtained camphoroxalic acid by the hydrolysis of the oil obtained by condensing camphor and ethyl oxalate. By the hydrolysis of the ether extract of the ethyl formate-camphor condensation Claisen's oxymethylenecamphor can be obtained. During this investigation compounds analogous to these have been isolated from the condensation of camphor with ethyl benzoate and with ethyl phthalate. No attempt has been made to purify the products obtained from the condensation of all of the above-named esters with camphor, this being beyond the scope of this investigation. It seems practically certain, from the results which have been accumulated, that these products are compounds similar in nature to camphoroxalic acid and oxymethylenecamphor. Enough work has been done, however, to show that their preparation in large quantities and in a pure form presents serious difficulties.

The experimental evidence shows that the reaction is markedly influenced by the nature of the ketone or aldehyde employed, and also by that of the ester. There is reason to doubt whether this influence is confined to a variation in the velocity. In some cases, at least, it seems to extend to the actual mechanism of the reaction. An effort has been made to obtain light on this point by a systematic study of the effect produced by variation in the constitution of the ester.

¹ Bishop, Claisen, and Sinclair: *Ann. Chem. (Liebig)*, **281**, 328.

² *Inaug. Diss., Munich*, 1889.

Until more work has been done on this subject it would be premature to generalize. It appears, however, that the readiness with which the reaction takes place is increased by the proximity of two carbethoxy groups. There is some evidence, which will be presented later, indicating the possibility that the mechanism of the reactions resulting in the formation of diketones is different in the case of the aliphatic and the aromatic esters.

E. The Catalytic Effect of Ether and the Tertiary Bases in the Claisen Condensation, and also in the Formation of the Grignard Reagent.—During a condensation of ethyl phthalate and camphor in ligroin solution, a little ether was added, because it had been observed that this condensation takes place much more rapidly when ether is used as a solvent. The reaction was at once accelerated to a marked degree. Because of this observation a series of experiments were undertaken, to throw light upon the catalytic action of ether and to find, if possible, other catalytic agents.

It was found that certain reactions, such for example as that between ethyl oxalate and camphor, take place readily and, apparently, with practically equal ease in ligroin or in ether solution. Others, such as that between ethyl phthalate and camphor, require many hours or days in ligroin solution, but take place easily when the materials are dissolved in ether. If a little ether be added to the ligroin solution, reaction begins at once and proceeds to completion. Apparently, the time required to carry the reaction to the end is dependent, other things being equal, on the amount of ether added. The position, then, is this, a given condensation can be accelerated or retarded by adding or withholding ether from the solution.

The question at once arises, Is this change in the velocity of the reaction due to a difference in the solvent action of the ether, or ether-ligroin mixture, as compared with the ligroin alone, or is it due to a difference of the temperature at which the reactions were carried out? As all the ligroin boiled at 36° , the experiments carried out at its boiling point were practically at the same temperature as those carried

out at the boiling point of ether. Actually, however, a majority of the experiments were carried out at the temperature of the room. In the discussion of the effect of different temperatures and solvents on the reaction, it was demonstrated that the difference cannot be accounted for by a difference in the solubilities of the products of the reaction in ether and in the other solvents employed.

A similar catalytic action of ether has been observed in one or two other cases. Prof. A. Michael has been good enough to point out that Menshutkin¹ was probably the first to show that the addition of ethyl iodide to trimethylamine takes place 200 times faster in ether than in ligroin. Freer,² from his experiments with sodium and acetone, which do not react except in the presence of a solvent of the latter, concludes that "ether is not an indifferent solvent."

Having established the specific action of ether as an accelerator of the condensation, an effort was made to discover other substances which might exert a similar influence. Two of these were found to be pyridine and quinoline, which appear to be about equal in their efficiency. Their influence is quite well defined, though it is not as great as that of ether. Experiments have been carried out in ligroin solution using a little of these substances as catalytic agents, and some condensations have also been made with pyridine alone as a solvent. The results were similar in all cases. When ethyl phthalate is condensed with camphor, the compound seems to exist in both the enolic and the ketonic forms. In this case, the use of pyridine or quinoline in the course of the condensation leads to a disturbance of the ordinary equilibrium in favor of the production of the ketonic form. This point is at present under investigation; should it prove to be substantiated it will be of considerable importance in the preparation of the class of bodies in question.

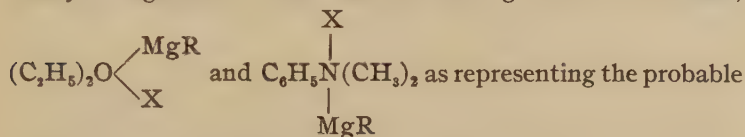
In a series of papers of great interest, W. Tschelinzeff³ has shown that the Grignard reagent is probably an oxonium derivative; that, at all events, as usually prepared, it contains

¹ J. Chem. Soc., 54, 901 (1888); Z. physik. Chem., 6, 41 (1890).

² Am. Chem. J., 15, 582 (1893); Bacon and Freer: *Ibid.*, 38, 367 (1907).

³ Ber. d. chem. Ges., 37, 2081, 4534; 38, 3664. Cf. Tingle: Am. Chem. J., 35, 94.

ether as an integral part of the molecule. He has also demonstrated that certain tertiary bases, such as dimethylaniline, can take the place of ether and, further, that although, in the absence of ether or of a tertiary base, the formation of the Grignard reagent does not take place at the temperature of boiling ether, yet it does so if the temperature be sufficiently raised, say to that of boiling benzene or toluene. He points out that both the ether and tertiary base act as typical catalytic agents in this reaction and gives the formulas,



constitution of the MgR ether compound and that of the tertiary base, respectively. It is at once evident that there is a close analogy between the results obtained with the Claisen condensation and the results of Tschelinzeff with the Grignard reagent. Accordingly a number of experiments were carried out to clear up certain points regarding which information was not available.

The conclusions reached may be briefly summarized as follows: The rapidity with which the magnesium is attacked by the halide compound is dependent on the nature of the alkyl or aryl halide employed, provided, of course, that other conditions remain constant. The presence of ether is not essential to the reaction, neither is a high temperature necessary, provided that sufficient time is allowed. A number of the experiments were carried out at the room temperature, in petroleum ether solution (b. p. 36°). The Grignard reaction admits of being controlled with the greatest ease. As is well known, its velocity can be increased by the use of ether, a tertiary base (pyridine, quinoline, etc.), or iodine, or by means of a high temperature (see above). The use of low-boiling ligroin, on the other hand, quickly diminishes the speed of reaction. In short, then, there appears to be a complete analogy in behavior between the Claisen condensation and the formation of the Grignard reagent.

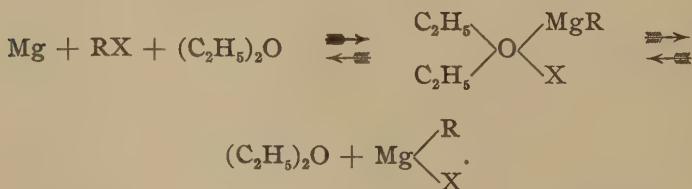
As regards the theory of the latter reaction a few remarks will be made which will follow the same general lines as the ideas of Tschelinzeff, although there are one or two points in his paper which seem to be not quite clear. The reaction

$\text{Mg} + \text{RX} \rightleftharpoons \text{Mg} \begin{smallmatrix} \text{R} \\ \diagup \\ \text{X} \end{smallmatrix}$ takes place with more or less difficulty, depending on the factors mentioned above. Grignard's reagent has the formula $\text{Mg} \begin{smallmatrix} \text{R} \\ \diagup \\ \text{X} \end{smallmatrix}$, i. e., ether is

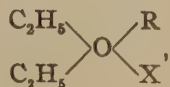
is not an essential constituent. The reaction represented above is greatly accelerated by the presence of a little ether which acts as a catalytic agent, forming an oxonium compound such as

$\begin{array}{c} \text{C}_2\text{H}_5 \\ \diagup \\ \text{O} \\ \diagdown \\ \text{C}_2\text{H}_5 \end{array} \begin{smallmatrix} \text{MgR} \\ \diagup \\ \text{X} \end{smallmatrix}$ (Tschelinzeff). Evidently,

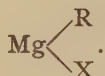
however, this is not the compound which necessarily reacts with the aldehyde, ester, etc., in the Grignard reactions; although, of course, in the presence of excess of ether it might be capable of doing so. It must, therefore, be an intermediate compound in equilibrium, as represented by the equation



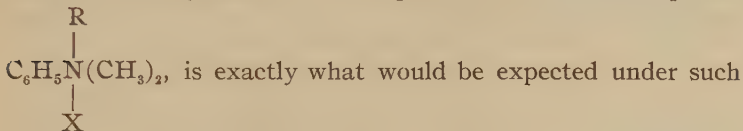
The question now arises, To what is the acceleration of the ether due? As it is difficult to see how it can have any effect on the magnesium metal, we can only regard it as favoring the dissociation of the alkyl halide into $\text{R} + \text{X}$ and, since the question is not one of dilution, there seems to be no escape from the conclusion that it forms the oxonium compound,



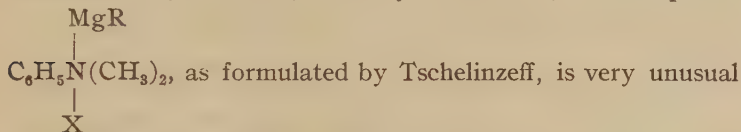
which would certainly be unstable and would, therefore, in all probability, unite quickly with the magnesium to form



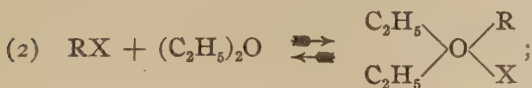
In support of this theory it may be pointed out that the corresponding reaction with a tertiary base, leading, in the case of dimethylaniline, to the production of the compound



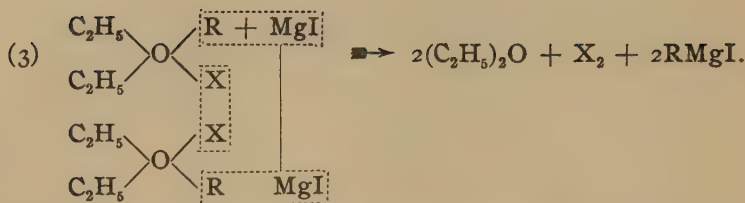
circumstances, whereas, to say the least, a compound



and without any special analogy. A further point for consideration is the effect of a trace of iodine which is so frequently added to start the attack on the magnesium. In view of the work of Baeyer and Villiger,¹ it can hardly be doubted that a magnesium subiodide, such as Mg_2I_2 , is first produced and that this then reacts with the oxonium compound formulated above. Of course, the magnesium is often attacked directly by the halide compound; to what extent this occurs obviously depends on the nature of the latter. To sum up, then, it may be considered that the acceleration in the formation of the Grignard reagent is dependent on such actions as are represented by the equations:



¹ Ber. d. chem. Ges., 36, 2775. Cf. Tingle: Am. Chem. J., 35, 95.



F. The Action of Ether and the Tertiary Bases on the Acetoacetic Ester Synthesis.—As is well known, ethyl acetoacetate is formed by condensing two molecules of ethyl acetate with one atom of sodium, using an excess of the ester as the solvent. The statement has been made by Higley¹ that in the presence of a solvent there is no trace of acetoacetic ester formed. Bacon,² on the other hand, whose results Higley claims to have confirmed, admits that traces of acetoacetic ester were obtained when ten parts of ether were used as a solvent.

In an interesting series of papers by Bouveault and Locquin,³ evidence is presented to show that, while ethyl acetoacetate is formed by the condensation of ethyl acetate and sodium when an excess of the ester is used as a solvent, when dissolved in benzene or ether the reaction results in the formation of the compound $\text{CH}_3\text{COCH}(\text{OH})\text{CH}_3$, after treating the product of the reaction with water. Similar compounds were also obtained by condensing esters of the higher aliphatic acids with sodium.

Some experiments on the acetoacetic ester condensation have been carried out, using as solvents small quantities of ether, petroleum ether (b. p. 36°), and pyridine. The catalytic effect of ether and pyridine on the velocity of the reaction is apparent. Moreover, when purifying the product in the manner described by Gattermann,⁴ there is obtained in each case a small amount of liquid which boils at 175° to 177° and gives an intense coloration with ferric chloride. The statement that no acetoacetic ester is formed in the presence of a solvent

¹ Am. Chem. Jour., **37**, 293.

² *Ibid.*, **33**, 77–80.

³ Bull. Soc. Chim., **36**, 629.

⁴ Prac. Meth. Org. Chem., 2nd Am. Ed., p. 155.

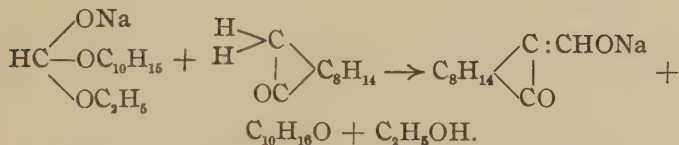
would seem to require verification. Furthermore, a long series of experiments fails to show that ether or the tertiary bases have any catalytic action when sodium reacts with es-

ters to form compounds of the class $\begin{array}{c} \text{C}_6\text{H}_5\text{CONa} \\ || \\ \text{C}_6\text{H}_5\text{CONa} \end{array}$. This would necessarily be the case here if only a compound of the above nature was formed.

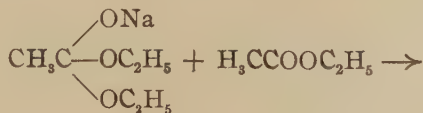
It seems probable that the two reactions take place simultaneously, and that in the presence of solvents the reaction $2\text{CH}_3\text{COOC}_2\text{H}_5 + 4\text{Na} \rightarrow \begin{array}{c} \text{CH}_3\text{CONa} \\ || \\ \text{CH}_3\text{CONa} \end{array} + 2\text{NaOC}_2\text{H}_5$ is by far the preponderating one.

G. *The Mechanism of the Reaction.*—The Claisen condensation is explained by its discoverer as follows:¹ When camphor and ethyl formate are condensed by means of sodium wire,

sodium borneolate and sodium camphor, $\text{C}_8\text{H}_{14} \begin{array}{l} \text{CH} \\ || \\ \text{CONa} \end{array}$, are first formed, and the latter, with the ester, yields the ortho compound, $\text{HC} \begin{array}{l} \text{ONa} \\ | \\ \text{OC}_{10}\text{H}_{16} \\ | \\ \text{OC}_2\text{H}_5 \end{array}$. This hypothetical intermediate product then reacts with camphor:



He explains similarly the acetoacetic ester synthesis, which is a special case of the Claisen condensation:



¹ Ann. Chem. (Liebig), **281**, 328.

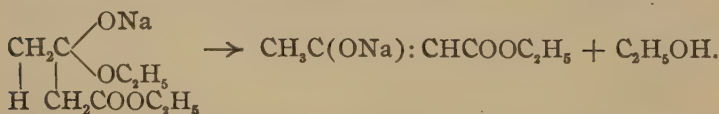
As seen from the above reactions, sodium ethylate is the active condensing agent. In the case of the acetoacetic ester synthesis a trace of alcohol is regarded as necessary to start the reaction. This reaction is cumulative because an increased amount of alcohol is being formed, and this, being acted upon by the sodium, gives an increasing amount of the active condensing agent—sodium ethylate. However, Claisen himself finds that sodium is a better condensing agent than sodium ethylate in alcoholic solution or sodium ethylate free from alcohol.

The explanation of the acetoacetic ester synthesis now advanced by Nef¹ is very similar to that of Claisen. The alcohol present in the ester forms sodium ethylate, and this reacts with ethyl acetate to form the intermediate compound

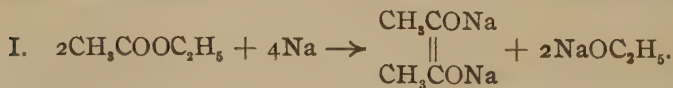
of Claisen, $\text{H}_3\text{C}-\begin{matrix} \diagup \text{ONa} \\ \text{---} \text{OC}_2\text{H}_5 \\ \diagdown \text{OC}_2\text{H}_5 \end{matrix}$. This substance is then supposed

to dissociate, giving $\text{CH}_2\text{C}-\begin{matrix} \diagup \text{ONa} \\ \text{---} \text{OC}_2\text{H}_5 \\ \diagdown \end{matrix}$ + $\text{C}_2\text{H}_5\text{OH}$.

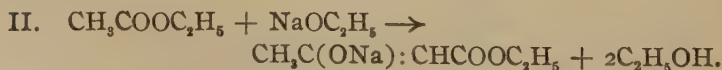
Another molecule of ester is assumed now to be added:



Higley² suggests that when ethyl acetate is treated with sodium two independent reactions take place simultaneously:



II. The sodium ethylate formed in (I.) reacts on the ethyl acetate as follows:



Here, again, it will be noted that sodium ethylate is the active condensing agent.

¹ Higley: *Am. Chem. Jour.*, **37**, 293.

² *Ibid.*

Higley concludes that this synthesis ought to give the best results when sodium ethylate is used as the condensing agent, as the reaction would then proceed entirely in the direction of the formation of acetoacetic ester until the point of equilibrium is reached, the reaction being a reversible one. This, he states, is reached when about 36.5 per cent of the acetoacetic ester has been formed. As found experimentally, however, the yield of the ester is not improved by the use of sodium ethylate, and, on the other hand, it is probable that sodium wire is the better condensing agent. This fact has been recorded by Claisen¹ and others, and the experiments herein described lead to the same conclusion.

Unless the superiority of sodium ethylate can be proved, the explanation of Higley is certainly not a logical one. Taking into consideration the present evidence as to the yield obtained in this synthesis when sodium and sodium ethylate are employed, if his explanation were correct, we should have the phenomenon of a condensing agent, formed at the expense of some of the ester used, proving more efficient than does the same agent when it is added to the original amount of the ester.

If the hypothesis of Claisen is correct, it is evident that sodium ethylate itself ought to be an excellent accelerator. This is found to be the case. In a series of experiments with camphor and the esters of various acids, using petroleum ether (b. p. 36°) as a solvent, the addition of a little alcoholic sodium ethylate accelerated a reaction to a marked degree. Absolute alcohol proved to be a still stronger accelerating agent. On the other hand, the use of sodium ethylate free from alcohol affected very little, if at all, the speed of the reaction. The most striking fact brought out by these experiments is the *great reduction in the yield of the diketone, when alcohol or alcoholic sodium ethylate is added to the reacting materials*. In the condensation of ethyl phthalate and camphor, the addition of two drops of alcoholic sodium ethylate reduced the yield of diketone about 50 per cent. The addition of a little alcohol causes an equally great reduction. A similar reduc-

¹ Ber. d. chem. Ges., **38**, 709.

tion was observed in every case where either of these reagents was used. When alcohol is employed it undoubtedly attacks some of the sodium, but this in no way accounts for the great reduction in the yield of the product; the solution of sodium in alcohol which was employed in our experiments had been treated with sodium until no more would dissolve.

Sodium ethylate free from alcohol did not materially decrease the yield of the diketone, but it is not as good a condensing agent as sodium wire. Claisen,¹ in his paper on oxy-methylenecamphor, states that alcoholic sodium ethylate is the weakest condensing agent, being followed in this respect by sodium ethylate free from alcohol and by sodium wire, in the order named. It has been experimentally established during this work that there is no difference in the solubility of sodium ethylate in ether, which was the solvent generally used by Claisen, and in the other solvents here employed. This is true of both the alcoholic solution of sodium ethylate and of that reagent free from alcohol.

Michael and others have pointed out that one of the weakest points in Claisen's explanation of the reaction which bears his name consists in the way in which he explains the influence exerted by sodium ethylate on the nature and extent of the changes involved. If sodium ethylate, or an analogous compound, is the active agent in promoting the condensation, then the addition of this compound should facilitate the reaction in question instead of retarding it. If the condensation is a reversible reaction this view would apply still more strongly. With regard to Claisen's claim that a trace of alcohol is necessary to start the reaction, it has already been pointed out that two drops of alcoholic sodium ethylate reduces the yield by nearly one-half, and that alcohol has a similar effect. It is hard to understand how it can reasonably be claimed that a reaction depends on the presence of a hypothetical trace of alcohol, when, as a matter of fact, the yield is so greatly reduced by the presence of the smallest tangible amount of the substance. The attempted explanation by Claisen² and by Higley³ of the

¹ *Loc. cit.*

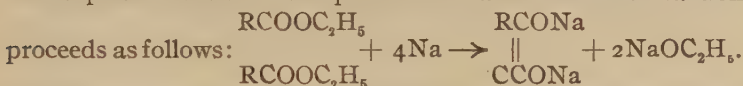
² *Ber. d. chem. Ges.*, **38**, 712.

³ *Loc. cit.*

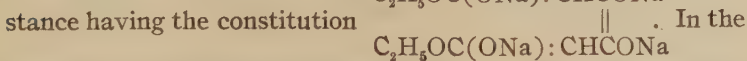
superior condensing power of sodium is, to say the least, not satisfactory.

A number of experiments have been carried out with the following objects in view: (a) To determine the effect of varying the amount of sodium used in the condensation. (b) To find out at what point in the condensation the catalytic agent exerts its accelerating influence. (c) To determine whether there is a difference in the mechanism of this reaction when aromatic esters are used instead of those of the aliphatic group.

Bouveault and Locquin¹ showed that when sodium acts upon the aliphatic esters in the presence of a solvent the reaction



The experiments with ethyl oxalate, herein described, show that this similarly combines with four atoms of sodium to one molecule of the ester. In the case of ethyl malonate, only two atoms of sodium will react with each molecule of the ester, and the first atom of the metal causes a generation of hydrogen while the second does not. In view of the reactions of the other esters of the aliphatic group, it is difficult to reconcile this reaction with the formula usually assigned to ethyl malonate. On the other hand, it has been suggested by various chemists that in some reactions its behavior accords better with the formula $\text{C}_2\text{H}_5\text{OC}(\text{OH})\text{:CHCOOC}_2\text{H}_5$.² If this hypothesis is correct we should expect that the first atomic proportion of sodium would liberate hydrogen from the hydroxyl group, and that the resulting compound, $\text{C}_2\text{H}_5\text{OC}(\text{ONa})\text{:CHCOOC}_2\text{H}_5$, would form, with another portion of the metal, sodium ethylate and a substance having the constitution



formation of camphoroxalic acid, J. Bishop Tingle³ found that the best yield resulted from the use of one atom of sodium and 1.5 molecules of camphor to one molecule of the ester, using ligroin

¹ *Loc. cit.*

² Cf. D. Vorlander: *Ber. d. chem. Ges.*, **36**, 268 (1903); E. Fischer and Dilthey: *Ibid.*, **35**, 844 (1902); Hans Meyer: *Ibid.*, **39**, 198 (1906).

³ *J. Chem. Soc.*, **57**, 652.

as a solvent. Wislicenus¹ has also studied the effect of an excess of sodium on ethyl acetate.

The experiments which have been performed in this investigation have brought out the following facts: When the esters of the aliphatic series are condensed with camphor, the use of more than one atomic proportion of sodium does not increase the yield of the diketone. The catalytic agent does not accelerate the reaction between sodium and the ester, nor between sodium and camphor. Sodium camphor is a weak condensing agent. Only traces of the acid involved are found in the products of the condensation.

When ethyl benzoate and camphor are condensed, two atoms of sodium combine with one molecule of the ester to give the

compound $\begin{array}{c} \text{C}_6\text{H}_5\text{CONa} \\ || \\ \text{C}_6\text{H}_5\text{CONa} \end{array}$, which is the product obtained by Nef²

upon treating benzil with sodium, and is analogous to the compound obtained by Bouveault and Locquin³ with the aliphatic esters. When this compound is treated with water, sodium benzoate and benzyl alcohol are formed in equimolecular proportions. Under suitable conditions, however, the hypothet-

ical product of hydrolysis, $\begin{array}{c} \text{C}_6\text{H}_5\text{COH} \\ || \\ \text{C}_6\text{H}_5\text{COH} \end{array}$, changes into benzoin,

$\text{C}_6\text{H}_5\text{CH}(\text{OH})\text{COC}_6\text{H}_5$; and this has been isolated in the form of its *m*-nitrobenzene derivative. The best yield of diketone is obtained when two atoms of sodium are allowed to react upon the ester, and sodium camphor is then added. When camphor was mixed with the reaction products of the ester with two atoms of sodium, the yield of the diketone was less than when the ester, camphor, and two atoms of sodium were allowed to react together.

The products obtained from the ethyl benzoate-camphor condensation are benzoic acid, benzyl alcohol, and the diketone. Apparently the formation of the diketone diminishes the amount of the benzyl alcohol obtained but does not affect the quantity

¹ Ann Chem. (Liebig), 186, 163.

² Ibid., 308, 287.

³ Loc. cit.

of benzoic acid formed. It was found that only traces of benzoic acid are produced from the hydrolysis of ethyl benzoate during the process used for the extraction of the diketone, so that the presence of the acid in the condensation product cannot be accounted for in this way. In the condensation of ethyl cinnamate and camphor a large quantity of the acid is also obtained in the product. In the condensation of ethyl phthalate, however, only traces of the acid are found.

These results seem to show that the mechanism of the reaction is not always the same. Nevertheless, the relative strength of the condensing materials employed, the effect of catalytic agents, and the influence of sodium ethylate and alcohol seem to extend to the condensation of esters of both the aliphatic and aromatic series.

It has been pointed out that the experimental facts obtained in this investigation cannot be reconciled with the theories of Claisen, Nef, and Higley concerning the mechanism of the reaction. An alternative theory, which was advanced by A. Michael,¹ may be expressed as follows: Sodium at first acts upon one molecule of ethyl acetate, displacing hydrogen,



This substance then reacts upon a second molecule of the

ester, giving the product $\text{CH}_3\text{C} \begin{array}{l} \nearrow \text{ONa} \\ \text{---} \text{OC}_2\text{H}_5 \\ \searrow \text{CH}_2\text{COOC}_2\text{H}_5 \end{array}$. Alcohol is

now eliminated with formation of the product $\text{CH}_3\text{C}(\text{ONa})\text{:CHCOOC}_2\text{H}_5$. When sodium ethylate is used as a condensing agent, it is assumed that it causes, by the loss of some of its energy, an aldol condensation, forming, for example,

the product $\text{CH}_3\text{C} \begin{array}{l} \nearrow \text{OH} \\ \text{---} \text{OC}_2\text{H}_5 \\ \searrow \text{CH}_2\text{COOC}_2\text{H}_5 \end{array}$. This then yields the ortho

sodium derivatives formulated above, and finally, by the loss of alcohol, ethyl sodioacetoacetate. Michael, later, adopted the view that the compound formed when sodium acts on ethyl

¹ Ber. d. chem. Ges., **33**, 3731; **38**, 1934.

acetate is $\text{CH}_2:\text{C}(\text{ONa})\text{OC}_2\text{H}_5$ instead of $\text{CH}_2\text{NaCOOC}_2\text{H}_5$. In view of recent work on tautomerism it seems likely that these two forms are in equilibrium.

The most striking differences between the two hypotheses appear to be the following: (1) Claisen assumes that it is not sodium itself which is the active agent, but a compound of the metal, such as sodium ethylate or sodium camphor; (2) The intermediate ortho compound is supposed by him to be an O- and not a C-derivative.

The reversal of the ethyl acetoacetate condensation, under the influence of sodium ethylate, has been studied very successfully by W. Dieckmann.¹ He shows that the velocity of the decomposition depends upon the degree of acidity of the particular β -ketonic ester employed. In conjunction with A. Kron,² in a paper which appeared while this article was in the press, he has also proved that the condensation may take place between esters and ketones of the type HCR_2CO . This fact is accounted for without difficulty by Michael's explanation of the acetoacetic ester condensation, but is incompatible with Claisen's theory. According to the latter the formation of the hypothetical intermediate compounds requires two atoms of hydrogen from the ketone, consequently the condensation can occur only between esters and ketones which contain the group H_3CCO or H_2CRCO .

With two reservations, noted below, the explanation of the mechanism of the condensation offered by Michael seems to be entirely satisfactory. The first reservation concerns the reaction of sodium on esters. Bouveault and his colleagues have proved how generally this reaction applies to compounds of the aliphatic series with the exception of ethyl acetate, which, as they have noted, acts in a different manner. It has been shown in the preceding pages that the reaction is the chief one which occurs with sodium and ethyl benzoate, in the presence of camphor; indeed, there can be no doubt that this, and not the Claisen condensation, is the preponderating reaction under the conditions described. It occurs, probably, in all cases where esters

¹ Ber. d. chem. Ges., **33**, 2670 (1900).

² *Ibid.*, **41**, 1260 (1908).

and sodium are brought together, its extent being determined by the nature of the ester and the experimental conditions. Obviously, these remarks, which are merely made for completeness, in no way modify Michael's explanation of the Claisen reaction itself.

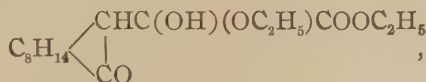
The second point to which attention must be called is the catalytic effect of ether and the tertiary bases. In considering this the following facts must be remembered: (1) The substances in question accelerate the Claisen condensation; (2) they act in the same manner in connection with the formation of the Grignard reagent (Grignard, Tschelinzeff); (3) ether facilitates the addition of ethyl iodide to triethylamine (Menschutkin); ether is markedly active in promoting the action of sodium on acetone (Freer); ether, as compared with petroleum ether, facilitates the action of sodium on ethyl acetate; ether is without effect on the interaction of sodium and ethyl benzoate.

The explanation already offered of the effect of ether and the tertiary bases on the formation of the Grignard reagent can be applied, *mutatis mutandis*, to cover, in a satisfactory manner, the points mentioned above. It postulates the formation of an oxonium compound, which, in the case of acetone, for example,

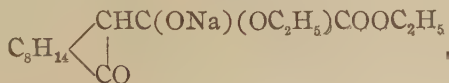
would be $\begin{array}{c} \text{C}_2\text{H}_5 \\ \diagup \\ \text{O} \\ \diagdown \\ \text{C}_2\text{H}_5 \end{array} \begin{array}{l} \text{H} \\ | \\ \text{OC}=\text{CH}_2 \\ | \\ \text{CH}_3 \end{array}$, whereas, with a ketone such as

camphor the formula $\begin{array}{c} \text{C}_2\text{H}_5 \\ \diagup \\ \text{O} \\ \diagdown \\ \text{C}_2\text{H}_5 \end{array} \begin{array}{l} \text{H} \quad \text{CH} \\ | \quad | \\ \text{O} \cdot \text{C} \quad \text{C}_8\text{H}_{14} \end{array}$ would apply. The

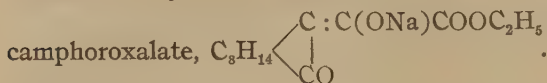
next step in the condensation of camphor with an ester, such as ethyl oxalate, for instance, would be, adopting Michael's formulation, the production of the compound



followed by that of the sodium derivative,



which then, by the elimination of alcohol, gives ethyl sodio-



The above oxonium derivatives might also be expected to be more reactive with sodium than compounds having the ordinary ketone structure. The essential point in the explanation which is offered is that it represents a change into a secondary form of the ketone.

EXPERIMENTAL.

Method of Experimentation.—Unless otherwise stated, the ketone and ester were dissolved in the solvent employed and the sodium was cut under another portion of the solvent and quickly transferred to the press. The wire was now rapidly forced into the flask containing the solution, the flask being then attached to a reversed condenser.

The product of the reaction was poured into ice water, the mixture well shaken, and the lighter layer removed and dried over calcium chloride. Then the solvent was distilled away. The material remaining after the distillation will be referred to in the following pages as the "solvent product." The aqueous solution obtained after the separation of the solvent was, in some cases, extracted with ether; but except in a few special instances this treatment was found to be without appreciable effect, and the practice was discontinued. The aqueous solution was next acidified and extracted four times with ether. The ethereal solution, after being dried over calcium chloride, was distilled. The residue which had been dissolved in the ethereal solution will be referred to as the "acidification product."

For the acidification, acetic, dilute hydrochloric, or dilute sulphuric acid was employed. Carbon dioxide was also used. No difference in the effect of these substances has been discovered, and consequently, in the later stages of the work, dilute hydrochloric acid was used. A number of chemists have employed acetic acid for the preparation of such compounds as we have investigated; the mineral acid is far more conve-

nient, and contamination of the "acidification product" with the excess of acetic acid extracted by the ether is avoided.

During the removal of the organic solvents by distillation the temperature was never allowed to rise above 100° , and was usually below this point. If necessary, the pressure was reduced.

A portion of the product of the reaction was dissolved in a few drops of ordinary alcohol (95 per cent). If alkali was present, the liquid was made faintly acid with pure, dilute hydrochloric acid. A few drops of an alcoholic solution of ferric chloride were added. The production of a reddish purple coloration was accepted as evidence of the formation of the enolic modification of the diketone.

The yields are sometimes referred to as "fair," "good," "poor," etc. It is a matter of regret that it has not been possible to be more definite on this point. Of course, the crude products of the reaction could have been weighed, and, in some cases, they were; but the figures obtained in this way would have been but little more definite and would probably have proved somewhat misleading. Reliable results can only be obtained by working out a method of purification for each individual compound, and it was impossible to attempt this because of the time required. The object has been to obtain general information and data, which could be used in a closer and more intensive study of these separate substances individually.

Preparation of Solvents and Reagents.—The solvents which have been employed were dried by means of sodium wire. When this was no longer tarnished, the liquid was decanted or filtered into a separate vessel, and a fresh portion of sodium wire was added. The solvent was allowed to remain in contact with this until used.

The esters were generally distilled, or their boiling points or melting points taken. Any free acid or acid ester was removed by washing with aqueous sodium hydroxide, and the compound was then dried by prolonged contact with calcium chloride.

The sodamide which was employed was made by the admirable method described by Winter,¹ which he worked out under the direction of Prof. Renouf.

¹ J. Am. Chem. Soc., **26**, 1484 (1904).

The metallic calcium was the commercial article, prepared electrolytically. This was turned to thin shavings on a lathe, the outer portion covered with oxide being discarded. The shavings were washed in dry ether, rapidly dried in warm air, and placed in a warm, dry bottle which was then sealed with paraffin. Under these conditions it remained bright for an indefinite time. The statement has been made¹ that the oxide adhering to the original sticks of the metal can be removed by immersion for a short time in 70 per cent alcohol. This plan was tried but the results were not encouraging.

The solution of sodium ethylate in alcohol was made by adding clean, bright sodium to absolute alcohol, suitably protected from moisture, until no more would dissolve.

Sodium ethylate free from alcohol was prepared by dissolving the sodium in a mixture of absolute alcohol and petroleum ether, the liquid being finally boiled for two hours to complete the reaction. It was now distilled until the contents of the flask were dry. The residue was quickly powdered and sifted, and used for further reactions as soon as possible after it was prepared.

The absolute alcohol was obtained by treating ordinary alcohol first with quicklime, then with dehydrated copper sulphate, and finally boiling it for several days with calcium turnings, from which it was eventually distilled. It was well protected from moisture and was used soon after its preparation.

The apparatus in which the condensation was carried out was carefully washed with alcohol and ether and dried by a current of hot air. During the whole course of the experiment the vessels in use were protected from moisture by means of calcium chloride tubes. Comparative experiments show that with some substances, at any rate, this latter precaution is unnecessary. It was adopted, however, in the case of all experiments which are described, unless otherwise stated expressly. It seems certain that the presence of traces of moisture is practically without effect on the condensation of some substances.

The sodium wire was obtained by placing clean, bright sodium

¹ Ber. d. chem. Ges., **38**, 3613 (1905).

in a sodium press and forcing it directly into the flask and solvent to be used for the condensation.

For the sake of brevity the work described in the following pages is given as if it were the result of single experiments. Actually, however, each experiment has been performed twice, and in many cases three or more times, until the evidence concerning the constancy and correctness of the observations made was satisfactory. Numerous changes were made in what may be termed the minor experimental conditions, but it has not been considered necessary to record these unless their results established some point which seems to be of importance.

EXPERIMENTS SHOWING THE EFFECT OF DIFFERENT CONDENSING AGENTS.

A. Experiments with Calcium Turnings.

Experiment 1.—22.8 grams camphor (1.5 mols.); 14.6 grams ethyl oxalate (1 mol.); 4.0 grams calcium (1 mol.); 400 cc. hexane (b. p. 90°).

After boiling for 40 minutes no signs of a reaction were observed. The addition of 25 cc. of absolute alcohol produced no effect. The solvent was distilled off and the condensation commenced immediately; after heating on a boiling water bath for one hour the calcium all disappeared. Two hundred cc. of petroleum ether were added and the product was extracted as usual. From the "acidification product" 10 grams of camphor-oxalic acid were obtained.

Experiment 2.—The same as Exp. 1, except that 50 cc. xylene were used as the solvent.

No action resulted from heating for three hours. The solvent was distilled off and the residue again heated for two hours at 200° without result. Upon adding 50 cc. absolute alcohol and heating at 100° for two hours the calcium was entirely dissolved. The product was extracted as in Exp. 1 and 10 grams of camphoroxalic acid were obtained.

Experiment 3.—The same as Exp. 1, except that 200 cc. of ether were used as the solvent.

No action took place during three hours at 36°. The addition of 75 cc. of pyridine produced no result.

Experiment 4.—22.8 grams camphor (1.5 mols.); 16.5 grams ethyl cinnamate (1 mol.); 4.0 grams calcium (1 mol.).

Boiling for two hours in 200 cc. hexane (b. p. 90°) produced no result. Fifty cc. of xylene were substituted for the hexane and the solution boiled for 4 hours without effect. When boiled for 4 hours at 160° without a solvent a reaction took place and part of the calcium was acted upon. The "acidification product" was a brown, semisolid mass. It was dissolved in ether and the solution extracted successively with aqueous solutions of sodium bicarbonate and sodium carbonate, cinnamic acid being thus removed. From the ethereal solution 5 cc. of a reddish brown oil were obtained which did not change after long standing. This gave a decided test with ferric chloride.

The "solvent products" obtained in the above experiment gave no tests with ferric chloride.

B. Experiments with Sodamide.

Experiment 5.—15.2 grams camphor (1 mol.); 14.6 grams ethyl oxalate (1 mol.); 3.9 grams sodamide (1 mol.).

No reaction resulted when hexane or xylene was used as solvents even when absolute alcohol was added. Upon heating for two hours without a solvent, at 150° , a reaction took place, a reddish brown mass resulting. From the "solvent" and "acidification products" were obtained 3 grams and 1 gram, respectively, of camphoroxalic acid.

Experiment 6.—The same as Exp. 5, using 200 cc. of ether and 75 cc. of pyridine as a solvent.

Boiling for 4 hours and standing at room temperature for some weeks produced no effect.

Experiment 7.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1 mol.); 3.9 grams sodamide (1 mol.); no solvent.

No reaction took place until the temperature was raised to 200° . The sodamide then disappeared within 5 minutes, and 5 cc. of a reddish brown oil giving a color test with ferric chloride were obtained. This gradually deposited benzoic acid. The residue consisted chiefly of ethyl benzoate. A small amount distilled at 230° to 245° . Very little condensation took place.

These experiments show that sodamide and calcium are far inferior to sodium unless the condensation takes place at a high temperature, at which the products must also be stable in order to obtain good yields.

EXPERIMENTS SHOWING THE EFFECT OF VARIOUS SOLVENTS AND TEMPERATURES.

A large number of condensations were carried out using as solvents varying quantities of ether, petroleum ether (b. p. 36°), ligroin (b. p. 50° to 55°), ligroin (b. p. 70° to 75°), hexane (b. p. 90°), benzene, toluene, and xylene. The esters used were ethyl formate, acetate, oxalate, benzoate, cinnamate, and phthalate. The products seemed equally soluble in all of the solvents and the solvent employed did not affect the yield of diketone obtained to any marked degree. The speed of the reaction seemed to increase with the temperature, except when ether was used as a solvent. In this case the reaction was accelerated to a marked degree, independently of the temperature.

EXPERIMENTS SHOWING THE EFFECT OF THE ESTERS OF VARIOUS ACIDS UPON THE CONDENSATION.

A. Aliphatic.

1. Esters of Monobasic Acids.

Experiment 9.—22.8 grams camphor (1.5 mols.); 7.4 grams ethyl formate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 300 cc. toluene.

After standing for a week at the room temperature, some of the metal remained unattacked. Consequently, the liquid was boiled for several hours. The yield of hydroxymethylencamphor was fair.

Claisen's experiments on the preparation of hydroxymethylenecamphor were made with ether as a solvent.

Experiment 10.—22.8 grams camphor (1.5 mols.); 8.8 grams ethyl acetate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 200 cc. ether.

The reaction commenced at room temperature, and at the end of twenty-four hours the liquid was dark brown, with a

brown precipitate at the bottom. There was also a dark brown solid having the general form of the wire, but examination showed that it contained very little sodium. The flask, with its contents, was allowed to remain eight days longer at the ordinary temperature, but no further change could be detected at the end of that time. The "solvent product" consisted of a yellow liquid which gave no coloration with ferric chloride. From this some camphor crystallized. The "acidification product" was a reddish brown oil, which did not solidify when placed in a freezing mixture, nor by long standing. It gave a deep color with ferric chloride. Treatment of its ethereal solution with aqueous solutions of sodium bicarbonate, sodium carbonate, and potassium hydroxide, in the order named, failed to remove any compounds. The exact details of this attempted method of separation are described under Experiment 14.

Experiment 11.—22.8 grams camphor (1.5 mols.); 11.6 grams ethyl butyrate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 200 cc. ether.

The action commenced at once at room temperature, and appeared to be complete at the end of about twelve hours. The solution was reddish brown in color, with a dark brown precipitate, partly in the form of pieces of the wire. The "solvent product," which gave no coloration with ferric chloride, deposited unchanged camphor. The "acidification product" consisted of a reddish brown oil, which gave a deep color with ferric chloride and did not solidify. Treatment with alkali and alkaline carbonates, in the manner described under Exp. 14, failed to yield any tangible products.

2. Esters of Dibasic Acids.

Work with the ethyl oxalate compound is described under Experiments 1 to 6. In addition, an exhaustive study of its action on camphor has been made by J. Bishop Tingle,¹ who has also investigated the behavior of the methyl, propyl, and isoamyl esters of the same acid.

Experiment 12.—22.8 grams camphor (1.5 mols.); 16.0 grams ethyl malonate (1.0 mol.); 4.6 grams sodium wire (1.0 atom); 300 cc. hexane (b. p. 90°).

¹ Am. Chem. Jour., **19**, 373 (1897); **20**, 318 (1898).

A brisk evolution of hydrogen accompanied the action of the sodium upon the ester in the hexane. It commenced immediately after the introduction of the wire into the solution. A white, flocculent material soon covered the metal, and the liquid became distinctly pink. The evolution of gas ceased after twenty minutes. The product was boiled for fifteen minutes longer, which caused the disintegration of the wire and its ultimate solution. The camphor, dissolved in a small quantity of hexane, was now added, whereupon the liquid began to turn brown. After two hours' boiling the precipitate had completely disappeared and the liquid was of a deep reddish brown color. It was allowed to remain overnight at the ordinary temperature.

The "solvent product" consisted of a black liquid, containing camphor; it gave no coloration with ferric chloride. The "acidification product," which was a heavy, reddish brown oil, gave a deep coloration with ferric chloride. The yield of oil was about 2 cc.

Experiment 13.—22.8 grams camphor (1.5 mols.); 17.4 grams ethyl succinate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 250 cc. ether.

After an hour at the room temperature, the substances showed no signs of reacting; but, on boiling, the liquid became yellow and a yellow incrustation formed over the wire. At the end of eight hours' boiling the metal began to disintegrate. Heating was now stopped and the material allowed to remain at the room temperature for forty-eight hours. The "solvent product" was a red liquid, which gave a coloration with ferric chloride and deposited camphor. The "acidification product" consisted of a reddish brown oil, which formed a deep colored solution with ferric chloride.

B. Aromatic.

1. Esters of Monobasic Acids.

Experiment 14.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1.0 mol.); 2.0 grams sodium wire (1.0 atom); 100 cc. hexane (b. p. 90°).

After two hours' heating on the water bath, the contents of the flask gradually became reddish brown. The material was

allowed to remain overnight at the ordinary temperature. The "solvent product" consisted of a yellow oil, which did not solidify and gave no test with ferric chloride. The "acidification product" was a reddish brown oil, which formed a deep color with ferric chloride. After some days most of the compound had solidified. It was dissolved in ether and the solution well shaken with aqueous solutions of sodium bicarbonate, sodium carbonate, and potassium hydroxide, successively. The residue from the ethereal solution was dried, the ether distilled off, and the resulting reddish brown oil, which gave no signs of solidification when kept in a freezing mixture for several days, was treated in the manner described below.

The three alkaline solutions were acidified and extracted separately with ether, which was then dried and distilled. In this manner there was obtained from the sodium bicarbonate solution a relatively large quantity of benzoic acid. The sodium carbonate solution was found to have extracted benzoic acid, together with a little yellow oil. A mere trace of yellow solid was extracted from the potassium hydroxide solution. None of these substances gave any red coloration with ferric chloride.

Returning now to the purified reaction product, which gave a deep coloration with ferric chloride and weighed 3.5 grams, it was mixed with water (50 cc.), and 10 cc. aqueous sodium hydroxide solution (sp. gr. 1.15) was added. After remaining at the room temperature for forty-eight hours, the solution was red, and a reddish brown, sticky substance had deposited. The liquid was poured off, acidified with dilute sulphuric acid, and allowed to stand overnight. In this manner a small quantity of crystals was obtained; extraction of the acid liquor did not materially increase the yield of these. A small additional quantity of the compound was obtained by a second treatment of the yellow, resinous material with aqueous alkali hydroxide. The solubility of the compound did not lend itself to its ready purification. After many trials it was found that the best results were obtained by the use of a mixture of acetone and water. In this manner, yellow, needle-shaped crystals melting at 91.5° were obtained. It gives a deep red color with ferric chloride. Analysis showed that the compound was not quite pure.

	Calculated for	
	$\text{C}_8\text{H}_{14}\begin{cases} \text{C}:\text{C}(\text{OH})\text{C}_6\text{H}_5 \\ \text{CO} \end{cases}$	
C	79.69	Found. 81.04
H	7.81	8.14

The investigation of this substance will be continued.

A number of attempts were made to obtain compounds of camphor with the ethyl nitrobenzoates. Sodium wire, alcoholic sodium ethylate, and sodium ethylate free from alcohol were employed as the condensing agents, and the temperature conditions were varied. It was found, in each case, that the last two condensing agents attacked the nitro group more or less vigorously, depending on the temperature. With sodium wire black compounds were formed. Apparently the hydrogen eliminated by the camphor reduced the nitro group to some extent, and the resulting products oxidized more or less on exposure to air.

Experiment 15.—22.8 grams camphor (1.5 mols.); 16.5 grams ethyl cinnamate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 500 cc. ether.

After the mixture had remained during ten minutes at the ordinary temperature the reaction had become very vigorous, and in the course of five minutes more, the sodium had dissolved completely. The liquid was a deep brown and a yellow, solid precipitate had formed; it was allowed to remain during twelve hours at the ordinary temperature.

The "solvent product" consisted of a reddish brown oil, which gave a decided coloration with ferric chloride. Before acidifying, the aqueous solution was again extracted with ether, to free it from traces of borneol and camphor, and the ether remaining in the aqueous solution was removed by a current of air. Acidification with acetic acid produced a milky precipitate, which, after twenty-four hours, had gathered on the dish in the form of a yellow, sticky mass that could not be filtered. The mother liquor was decanted and the material dried. It gave a deep coloration with ferric chloride.

2. Esters of Dibasic Acids.

Experiment 16.—22.8 grams camphor (1.5 mols.); 22.2 grams ethyl phthalate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 300 cc. ether.

Immediately after mixing the materials the wire turned dark, and in the course of a few minutes the reaction was so violent that it was necessary to moderate it by immersing the flask in ice water. The wire had completely dissolved at the end of fifteen minutes, the solution assuming a golden brown color. It was allowed to stand overnight at the room temperature.

The liquid was poured into ice water, the mixture well shaken, and the ether removed. After evaporation it left a red liquid which gave a slight coloration with ferric chloride. The aqueous solution was extracted twice with fresh portions of ether and it was then treated with a current of air, until it no longer gave an odor of ether. Dilute acetic acid (1:1) was now added in excess. A yellow, sticky substance separated immediately; it was allowed to remain in contact with the mother liquor for twenty-four hours and was then filtered. After being dried it formed a yellow resin, was readily soluble in alcohol, and gave a deep coloration with ferric chloride. The acid mother liquor was extracted with ether. This extract left a quantity of reddish brown oil which gave an intense coloration with ferric chloride. This oil, in the course of a week, changed almost completely into a white solid which gave no coloration with ferric chloride. The resinous material spoken of above also changes slowly into a white solid giving no reaction with ferric chloride. It appears as if there were here an unstable enolic and a stable ketonic form of the diketone, which produce an equilibrium mixture after the liberation of the former. The supposed ketonic form is insoluble in alcohol, ether, and benzene. The supposed enolic form is soluble in all of these. If the enolic form is dissolved away from an equilibrium mixture of the two forms, it will slowly commence to deposit more of the supposed ketonic form.

This substance is now under investigation.

INFLUENCE OF CATALYTIC AGENTS ON THE CLAISEN CONDENSATION.

Experiment 17.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 400 cc. petroleum ether (b. p. 36°).

An action commenced slowly at the room temperature. The wire continued bright or white for two hours, during which time a yellow precipitate deposited in the flask. The liquid now became yellow and gradually darkened, finally becoming deep red. The wire also darkened and acquired a reddish brown coating, but five days were required before it disappeared. The solution and precipitate were treated separately with water, acid, etc. About equal amounts of the "acidification products" of the solution and the precipitate were obtained. They consisted chiefly of benzoic acid, together with a reddish brown oil which gave a coloration with ferric chloride. The "solvent product" was a yellow oil which gave a coloration with ferric chloride. The yield of diketone was poor, about 4.0 grams of the crude diketone and 2.3 grams of benzoic acid being formed.

Experiment 18.—Same as Exp. 17. Added as a catalytic agent 100 cc. ether.

A reaction commenced at once, and after about an hour the solution had about the same color as described in Exp. 25, but the precipitate was not quite as heavy and the coating on the wire was much thicker. At the end of two hours all but a slender thread of sodium had disappeared; the liquid was deep red and the precipitate a very deep brown. It was allowed to remain overnight. The yield of diketone was about the same as that obtained in Exp. 17.

Experiment 19.—Same as Exp. 17. Added as a catalytic agent 75 cc. pyridine.

The liquid quickly assumed a bluish tinge, the wire acquired a dark coating, and there was a small quantity of a white, flocculent precipitate. At the end of two hours this precipitate had disappeared, but another one, almost black, had collected at the bottom of the flask. The liquid was reddish brown, and the metal had almost all reacted. The mixture was allowed to remain overnight. The yield was practically the same as in the preceding experiments and the velocity of the reaction essentially equal to that produced by ether.

Experiment 20.—Same as Exp. 17. Added as a catalytic agent 10 cc. quinoline.

The reaction commenced at once. The liquid and wire both darkened and the metal became covered with a rough coating, a brown precipitate being also deposited on the bottom of the flask. The liquid was boiled during two hours, at the end of which time most of the metal had reacted. The product was allowed to remain overnight. The yield was practically identical with that obtained in the previous experiments.

Experiment 21.—22.8 grams camphor (1.5 mols.); 16.5 grams ethyl cinnamate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 500 cc. ether.

After remaining for ten minutes at the ordinary temperature the reaction had become quite brisk, and at the end of five minutes more the sodium had disappeared. The liquid was deep brown with a yellow solid which did not adhere to the metal. The "solvent product" consisted of a yellow oil. The "acidification product" was, at first, entirely liquid, but gradually deposited a red, sticky solid which was removed. All three products gave deep colors with ferric chloride.

Experiment 22.—The same quantities of camphor, ester, and sodium as in Exp. 29; 300 cc. petroleum ether (b. p. 36°).

Hardly any action had taken place at the end of two hours, consequently, 25 cc. of ether were added. This caused the rapid production of a red solid, the wire remaining bright throughout the experiment. At the end of two hours most of the metal had dissolved and the remainder disappeared after the mixture had been allowed to stand overnight. The yield was practically the same as in the preceding experiment.

Experiment 23.—22.8 grams camphor (1.5 mols.); 22.2 grams ethyl phthalate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 400 cc. petroleum ether (b. p. 36°).

During six hours at room temperature, the wire gradually darkened and assumed a brown coating, which then slowly deposited at the bottom of the flask. The liquid became yellow. After remaining overnight practically all the sodium had reacted, but much of the solid product retained the original form of the wire coils. The yield was as good as any which has been obtained.

Experiment 24.—Same as Exp. 23. Added as a catalytic agent 50 cc. ether.

The mixture without the ether was allowed to remain for an hour at room temperature. The ether was then added. The action immediately became more rapid, and at the end of three hours the metal had completely disappeared and a finely divided, dark brown precipitate had formed. This was allowed to remain during twenty-four hours at the room temperature. The yield of diketone was about equal to that previously obtained.

Experiment 25.—Same as Exp. 23. Added as a catalytic agent 10 cc. of quinoline.

In five minutes the wire became red, and at the end of three hours all of it except a thin thread had reacted. The liquid was reddish brown, and a black precipitate had formed. A good yield of the product was obtained, but it appeared to consist entirely of what is believed to be the ketonic form of the diketone. Although the reaction did not take place as rapidly as when ether was employed as the catalyst, there is no doubt as to the large accelerating influence of quinoline.

Experiment 26.—Same as Exp. 25, except that ethyl oxalate was used instead of ethyl phthalate.

The object of this experiment was to see if quinoline had any influence on the production of (enolic) camphoroxalic acid. The product, however, appeared to be identical with the ordinary form of the acid. In view of Michael's investigation of the action of tertiary bases and desmotropic compounds,¹ this result is what might be expected.

Experiment 27.—Same as Exp. 23. Added as a catalytic agent 100 cc. pyridine.

This experiment was performed to see if pyridine, as well as quinoline, tended to promote the formation of the supposed ketonic form.

At the ordinary temperature the wire and liquid immediately darkened, and a black precipitate formed. After an hour almost all the sodium had dissolved, and the following morning it had completely disappeared. Neither of the products of this

¹ Ber. d. chem. Ges., **39**, 209 (1906).

reaction gave any coloration with ferric chloride. The catalytic influence of pyridine was plainly evident.

INVESTIGATION OF CONDITIONS AFFECTING THE FORMATION OF THE GRIGNARD REAGENT.

The object of these experiments was to discover whether the Grignard reagent can be formed under certain conditions, at a relatively low temperature, in the absence of ether or a tertiary base. For this purpose it was, obviously, desirable to use a halogen derivative which possessed the maximum activity toward magnesium. Some of our experiments were made with ethyl chloracetate, which was found to be well adapted to our purpose.

Experiment 28.—12.0 grams ethyl chloracetate (2 mols.); 1.22 grams magnesium ribbon (1 atom); 50 cc. ether.

The reaction took place so rapidly that it was necessary to cool the materials in a freezing mixture.

Experiment 29.—This was the same as Exp. 28, except that 200 cc. petroleum ether (b. p. 36°) were used in place of the ether. No apparent action was observed after several hours' boiling, consequently a little iodine was added and the heating continued for ten hours longer. The liquid had turned yellow at the end of this time, and a yellow, crystalline precipitate coated the metal and settled to the bottom of the flask.

Experiment 30.—The conditions were the same as in Exp. 29, except that the solvent consisted of 35 cc. of ether in addition to the petroleum ether. After three hours' boiling a heavy precipitate had formed and at the end of ten hours this was largely augmented. Action was much more rapid than in the preceding experiment.

Experiment 31.—This was carried out exactly as in the case of Exp. 29, except that the solvent petroleum ether was reduced to 50 cc. Most of the magnesium had dissolved after boiling for sixteen hours. Evidently a greater concentration of the ester favors its attack on the metal.

Experiment 32.—7.80 grams ethyl iodide (1 mol.); 1.22 grams magnesium ribbon (1 atom); 50 cc. petroleum ether (b. p. 36°); 30 cc. quinoline.

No reaction took place at the ordinary temperature, but after boiling for twenty minutes most of the metal had dissolved and a red mass formed. With benzoic aldehyde this substance gave a rather poor yield of the secondary alcohol.

Experiment 33.—This was similar to the preceding experiment, except that 25 cc. of ether were used instead of the quinoline, and the quantity of petroleum ether was reduced one half. The action commenced at the ordinary temperature, the liquid soon began to boil, and after half an hour most of the metal had dissolved. Treatment of the product with benzoic aldehyde gave an excellent yield of the secondary alcohol.

Experiment 34.—7.80 grams brombenzene (1 mol.); 1.22 grams magnesium ribbon (1 atom); 200 cc. petroleum ether (b. p. 36°); 5 cc. quinoline.

No apparent change took place after two hours' boiling; consequently, a little iodine was added and the heating was continued during ten hours. A red compound was formed, which reacted only slowly with benzoic aldehyde, and the yield of secondary alcohol was poor.

Experiment 35.—This was a repetition of the preceding experiment, but 50 cc. of pyridine were used instead of the petroleum ether and quinoline. The results were similar to those recorded above, except that the metal had almost all disappeared after four hours' boiling.

Experiment 36.—A similar experiment to Exp. 34, except that the quantity of petroleum ether was reduced to 50 cc. and 15 cc. of pyridine were added as the catalytic agent. Most of the metal had dissolved after six hours' boiling. The product of the reaction was similar to those described above.

EFFECT OF SOLVENTS AND CATALYTIC AGENTS ON THE SYNTHESIS OF ETHYL ACETOACETATE.

Under ordinary conditions the synthesis of ethyl acetoacetate, as is well known, is carried out by the use of ethyl acetate in excess, the excess acting as the solvent. It was desired to ascertain the effect upon the reaction of the use of petroleum ether as a solvent, and also to determine the action of catalytic agents such as ether and pyridine.

Experiment 37.—17.6 grams ethyl acetate (2 mols.); 2.3 grams sodium wire (1 atom); 50 cc. petroleum ether (b. p. 36°).

During the first half hour a slight reaction took place, some white, flocculent matter was formed and then disappeared, and there was a slight evolution of hydrogen. The liquid turned yellow gradually, but there was no further change during fourteen hours at the room temperature. After four days under the same conditions the liquid was darker. The wire retained its form, although most of the metal had reacted. The product of the reaction was treated in the manner described by Gattermann.¹ After purification a portion boiled at 175° to 177° and this gave an intense color with ferric chloride.

Experiment 38.—This was the same as the preceding experiment except that 75 cc. of ether were added. The reaction was much more rapid than before. The mixture was allowed to remain during twelve hours at the ordinary temperature, then boiled for four hours, at the end of which time all the sodium had reacted. After remaining overnight the ethyl acetoacetate was separated and identified as described above.

Experiment 39.—In this case 35 cc. of ether were employed; otherwise the conditions were the same as in Exp. 37. The reaction was more rapid and a considerable quantity of the metal was dissolved during the first hour. It was allowed to remain overnight and then boiled for four hours. The product gave the same tests as in the preceding cases.

Experiment 40.—This was also the same as Exp. 37, except that 35 cc. of pyridine were added. At the end of an hour, at the ordinary temperature, the liquid was red, with some dark colored material at the bottom. After remaining overnight it was heated for two hours, when the sodium had, apparently, all reacted. The product gave the tests previously noted.

Experiment 41.—17.6 grams ethyl acetate (2 mols.); 2.3 grams sodium wire (1 atom); 35 cc. pyridine.

A reaction commenced immediately, the wire gradually becoming red, then black and, after heating during two hours, the sodium was completely changed. The product was freed from pyridine by washing with dilute (1:3) hydrochloric acid and

¹ Organ. Prep., 2nd Am. Ed., p. 155.

subsequently distilled under reduced pressure. The purified material gave the tests for ethyl acetoacetate.

EFFECT ON THE CLAISEN CONDENSATION OF THE PRESENCE OF ALCOHOL OR OF SODIUM ALCOHOLATE.

A. Solubility of Alcoholic Sodium Ethylate and of Sodium Ethylate Free from Alcohol.

No statement has been found regarding the solubility of these substances and, consequently, some qualitative determinations have been made in order to be in a position to judge as to whether its behavior was due primarily to changes of solubility in the varying solvents employed.

The alcoholic sodium ethylate was mixed with an equal volume of each of the following substances: Dry ether free from alcohol, petroleum ether (b. p. 36°), ligroin (b. p. 80°), hexane (b. p. 90°), toluene. No precipitate formed after remaining for an hour nor on heating the liquids. In all cases the solutions remained homogeneous.

Sodium ethylate free from alcohol, in a finely powdered condition, was added, in small quantity, to separate portions of each of the following liquids: Dry ether free from alcohol, petroleum ether (b. p. 36°), ligroin (b. p. 80°), hexane (b. p. 90°), benzene, pyridine, quinoline. In no case did any appreciable quantity dissolve.

B. Experiments on the Synthesis of Ethyl Acetoacetate.

Experiment 42.—17.6 grams ethyl acetate (2 mols.); 2.0 grams sodium wire (1 atom); 50 cc. petroleum ether (b. p. 36°); 10 drops of alcoholic sodium ethylate.

An action commenced at once, the sodium turning white and the liquid darkening rapidly. After remaining for an hour at the ordinary temperature, the liquid was boiled for two hours, at the end of which time the sodium had disappeared. The product gave traces of ethyl acetoacetate, as shown by the boiling point test and the coloration with ferric chloride.

Experiment 43.—17.6 grams ethyl acetate (2 mols.); 6.8 grams sodium ethylate free from alcohol (1 mol.).

The ester was added to the sodium ethylate without removing

the latter from the flask in which it had been prepared. When heated on a water bath the solid turned brown and dissolved gradually. After ten hours one half of the product was removed and tested for ethyl acetoacetate, which was found to be present only in traces. To the remaining portion of the product 50 cc. of ether were added and the heating continued for ten hours longer. There was no change in the appearance of the material, but it yielded 2.5 grams of a liquid which boiled at 175° to 177° and gave a deep coloration with ferric chloride. This yield is 27 per cent of the theoretical, whereas, by the ordinary method the yield is about 30 per cent. The increased yield in the second part of the experiment is attributed to the catalytic action of the ether and not to the extra heating.

C. Experiments with Ethyl Benzoate.

Experiment 44.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1.0 mol.); 2.3 grams sodium (1.0 atom); 200 cc. petroleum ether (b. p. 36°); 25 cc. alcoholic sodium ethylate.

The liquid darkened immediately, and after ten minutes began to boil. The action was complete after thirty minutes, the liquid being dark, with a reddish brown solid at the bottom of the flask. It was allowed to remain overnight. The "solvent product" was a yellow oil which gave no coloration with ferric chloride. The "acidification product" consisted chiefly of benzoic acid, together with a very little diketone. The acid was extracted by means of an aqueous solution of sodium bicarbonate.

Experiment 45.—15.0 grams camphor (1 mol.); 15.0 grams ethyl benzoate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); absolute alcohol.

The metal was dissolved in four times the theoretical quantity of absolute alcohol. The camphor was dissolved in the ethyl benzoate. The solutions were mixed, but no visible reaction took place. Heating on a water bath caused the deposition of a white, solid cake, which was completely dissolved at the end of two hours, the solution becoming gradually dark. The "solvent product" was similar to that obtained in the preceding experiment. The "acidification product" consisted of

a red oil which gave no characteristic coloration with ferric chloride. It proved to consist almost entirely of ethyl benzoate, together with traces of benzoic acid.

Experiment 46.—22.8 grams camphor (1 mol.); 15.0 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (1 atom); 6.9 grams dry sodium ethylate; 200 cc. petroleum ether (b. p. 36°).

After mixing the materials the liquid became slightly dark at the ordinary temperature, during the course of an hour. It was allowed to remain overnight without heating, and was then dark brown, with a heavy, yellow precipitate. Most of the sodium had disappeared. The contents of the flask were treated in the usual manner. The "solvent product" resembled that in the two preceding experiments. From the "acidification product" some benzoic acid separated, together with 1.2 grams of diketone.

Experiment 47.—This was the same as Exp. 44, except that 25 cc. of absolute alcohol were used in place of the same volume of alcoholic sodium ethylate. The reaction commenced at once and the liquid began to boil violently at the end of three minutes, so that it was necessary to immerse the flask in ice water. The action appeared to be complete after fifteen minutes. The "solvent product" resembled that obtained in Exp. 44. The "acidification product" consisted chiefly of ethyl benzoate, together with a relatively large quantity of benzoic acid. The quantity of diketone formed was very small.

D. Experiments with Ethyl Phthalate.

Experiment 48.—22.8 grams camphor (1.5 mols.); 22.2 grams ethyl phthalate (1 mol.); 2.3 grams sodium wire (1 atom); 400 cc. petroleum ether (b. p. 36°); 25 cc. alcoholic sodium ethylate.

A reaction commenced immediately, the wire and the liquid both turning dark. After fifteen minutes at the room temperature about half of the wire had dissolved. Action appeared to be practically complete at the end of two hours. The liquid was dark red, most of the wire had disappeared, and the remainder had entirely disintegrated. The "solvent product" was a yellow oil. Both it and the "acidification product" gave

a red color with ferric chloride, but the yield of the "acidification product" was only about one half of that obtained, under similar conditions, by the use of ether or a tertiary base as a catalytic agent.

Experiment 49.—This was the same as Exp. 48, except that only two drops of alcoholic sodium ethylate were employed. About four hours were required to complete the reaction. The product and the yield were practically the same as in the preceding experiment.

Experiment 50.—This was the same as Exp. 48, except that the alcoholic sodium ethylate was replaced by an equal volume of absolute alcohol. The sodium wire remained light colored for two minutes and then commenced to darken rapidly; two minutes later it was brown and the liquid reddish in color, and there was a considerable evolution of gas or vapor from the neighborhood of the wire. Fifteen minutes after the experiment was commenced the metal had disappeared and the liquid had assumed a deep reddish tint. It was allowed to remain overnight at the ordinary temperature. The "solvent product" was a yellow oil, which gave no coloration with ferric chloride. The "acidification product" consisted of about 3 cc. of a reddish brown oil, giving a deep color with ferric chloride. The oil rapidly changed to a white solid. The yield of condensation product was much smaller than that obtained in Exp. 48, where alcoholic sodium ethylate was used.

These results show that although a reaction is rapidly brought about by the use of alcoholic sodium ethylate, and even more rapidly by the use of absolute alcohol, yet the yield of diketone is diminished in every case and relatively large quantities of benzoic acid are obtained. Apparently no phthalic acid is formed under similar conditions. It is hoped that more light on this interesting point will be gained in a subsequent investigation.

THE EFFECT OF VARYING QUANTITIES OF SODIUM ON THE YIELD OF DIKETONE.

These experiments were carried out in connection with the ones described in the following section. Those esters were se-

lected which had been found to react the most readily with sodium. Bishop Tingle has described some work regarding the effect produced on the yield of camphoroxalic acid by varying proportions of sodium, and J. Wislicenus¹ studied the action of sodium, in excess, on ethyl acetate.

Experiment 51.—7.9 grams camphor (1 mol.); 7.3 grams ethyl oxalate (1 mol.); 4.6 grams sodium wire (4 atoms); 250 cc. hexane (b. p. 90°).

The wire was added to the ester and the solvent, and the mixture heated for about fifteen hours. At the end of this time the metal had reacted. The liquid was reddish brown and a red precipitate had formed. The camphor, dissolved in the remaining hexane, was now poured in and the heating continued for four hours. Most of the solid dissolved. The "acidification product" gave 5.3 grams of camphoroxalic acid, or 43 per cent of the theoretical yield. This is only about half the average yield obtained when one atomic proportion of sodium is added.

Experiment 52.—7.6 grams camphor (1 mol.); 7.3 grams ethyl oxalate (1 mol.); 2.3 grams sodium wire (2 atoms); 250 cc. ether.

Only one half the above quantity of sodium was added at first to the ester and the solvent. The reaction proceeded as in Exp. 51. The ether did not appear to affect the speed of the reaction between sodium and the ester. After heating during two hours on a water bath the wire retained its shape; the liquid was yellow, and a precipitate of the same color had formed. The remaining sodium was now added together with the camphor, the solution having been cooled to the room temperature. At the end of three minutes the liquid boiled and in twenty minutes the action ceased, although much of the wire still held its shape. The product was boiled for twenty minutes more and allowed to remain at room temperature for twelve hours. This treatment produced no visible change. Before the addition of the product to water and acid, about a gram of unchanged sodium was removed. The yield of crude camphoroxalic acid was 5.5 grams, which is 58 per cent of the theoretical.

¹ Ann. Chem. (Liebig), 186, 193 (1877).

Experiment 53.—7.6 grams camphor (1 mol.); 8.0 grams ethyl malonate (1 mol.); 2.3 grams sodium wire (2 atoms); 250 cc. hexane (b. p. 90°).

As soon as the evolution of hydrogen, caused by adding the sodium to the ester and solvent, had ceased, the mixture was heated on a water bath during four hours, and then allowed to remain overnight at the ordinary temperature. A white, flocculent compound was present in the liquid, but much of the wire was unchanged. The mixture was boiled on a sand bath during twenty hours, at the end of which time about one half of the wire was unchanged. The liquid was yellow and the precipitate brown. The camphor, dissolved in hexane, was now added and the heating continued for four hours. The product was allowed to stand overnight. Some of the sodium was still unchanged; the liquid was a deep reddish brown, with a dark precipitate present. The "acidification product" consisted of 3.8 grams of a reddish brown oil which gave an intense color with ferric chloride.

Experiment 54.—8.75 grams sodium camphor (1 mol.); 8.00 grams ethyl malonate (1 mol.); 2.30 grams sodium wire (2 atoms); 300 cc. petroleum ether (b. p. 36°); 50 cc. ether.

The ester, one half the sodium, and the petroleum ether were mixed and allowed to remain at the room temperature during twelve hours. The mixture was then boiled for two hours, when the metal was dissolved. The remaining sodium was now added and the boiling continued. A yellow solid formed gradually. More sodium was then put in, but as it remained unchanged it was removed later. The sodium camphor and ether were now added. After boiling for six hours the solid was a deep brown. It was allowed to remain overnight. The "acidification product" consisted of 2.4 grams of oil, which gave an intense coloration with ferric chloride.

Experiment 55.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (1 atom); 50 cc. hexane (b. p. 90°).

The camphor, sodium, and solvent were mixed and heated for an hour. The product was light yellow, but on adding the ester it rapidly became brown. It was heated for another

hour. The "acidification product" was a white solid (benzoic acid), with a little reddish brown oil. The yield of diketone was poor.

Experiment 56.—11.4 grams camphor (1.5 mols.); 7.5 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (2 atoms); 300 cc. ligroin (b. p. 70°); 50 cc. ether.

After remaining for three hours at the ordinary temperature the wire was dark brown; it was boiled during four hours and allowed to remain overnight. The liquid was yellow and a brownish yellow precipitate had formed. After being heated for two hours longer and allowed to remain at the ordinary temperature for twenty-four hours, the wire had almost completely changed and most of the product was in solution. The "acidification product" consisted of 5.3 grams of a yellow solid, from which 2 grams of benzoic acid were separated by means of an aqueous solution of sodium bicarbonate, after dissolving the product in ether. The residual diketone weighed 0.7 gram. The "solvent product" was distilled with steam. The volatile material consisted of 2.1 grams of benzyl alcohol and 6.0 grams of a mixture of camphor and borneol. The nonvolatile portion failed to react with phenylhydrazine or with *m*-nitrobenzoyl chloride and alkali.

Experiment 57.—This was a duplicate of the preceding experiment, except that twice as much sodium wire was employed. The reaction proceeded in the manner described. The "solvent product" yielded a little camphor and borneol, but only traces of benzyl alcohol. The "acidification product" consisted of 8.3 grams of solid, which gave 2.7 grams of benzoic acid and 2.2 grams of crude diketone.

Experiment 58.—The quantities of substances used were the same as in Exp. 57, but the two atomic proportions of sodium were allowed to react with the ester. After two hours' heating the liquid was yellow, with a red precipitate present; the wire was golden brown. The heating was continued for six hours longer, when the precipitate was light brown and the liquid yellow. Almost all of the sodium had reacted. The camphor was now added and the heating continued dur-

ing seven hours. The solvent was yellow and the precipitate a deep reddish brown. The "solvent product" gave 4.4 grams of camphor and borneol, and only traces of benzyl alcohol. The "acidification product" consisted of 12.8 grams of reddish brown oil, from which 3.8 grams of benzoic acid and 1.0 gram of crude diketone were separated.

Experiment 59.—7.6 grams camphor (1 mol.); 7.5 grams ethyl benzoate (1 mol.); 6.9 grams sodium wire (3 atoms); 300 cc. ligroin (b. p. 70°); 50 cc. ether.

The ester was treated with two thirds of the sodium and the camphor with the remainder. In neither case did the ether appear to exert a catalytic influence. When the products were mixed no change took place at the ordinary temperature. After heating during seven hours, the liquid was reddish brown, with a dark brown precipitate present. The "solvent product" was a yellow oil, consisting mainly of the higher-boiling solvent. Benzyl alcohol could not be detected. The "acidification product" consisted of 7.5 grams of a reddish brown oil, from which 3.0 grams of benzoic acid and 4.4 grams of the crude diketone were obtained.

ACTION OF SODIUM ON ETHYL BENZOATE.

Bouveault's interesting work on the interaction of sodium and the aliphatic esters has been referred to previously. The action of sodium on ethyl benzoate has been investigated by Claisen and others. The main object of these experiments was to try to gain additional knowledge regarding the nature and reaction of the products formed from the metal and ester.

Experiment 60.—13.7 grams ethyl benzoate (1 mol.); 2.1 grams sodium wire (1 atom); 19.85 grams absolute alcohol; 200 cc. petroleum ether (b. p. 36°).

An action commenced at once. Hydrogen was, of course, evolved and the solution darkened rapidly. At the end of an hour most of the metal had reacted; the solution was reddish brown and a light colored precipitate was present. The flask was allowed to remain at room temperature for two hours longer. The "solvent product" consisted of a yellow oil from which 9.7 grams of ethyl benzoate were obtained, but

no benzoic acid. The "acidification product" gave 2.6 grams of benzoic acid, equivalent to 2.3 grams of the ester. This leaves 0.9 gram of the ester unaccounted for.

Experiment 61.—15.0 grams ethyl benzoate (1 mol.); 4.6 grams sodium wire (2 atoms); 4.6 grams absolute alcohol (1 mol.); 2.3 grams sodium wire (1 mol.), to form sodium ethylate; 14.2 grams camphor (1 mol.); 200 cc. ligroin (b. p. 90°); 50 cc. ether.

The solvent and the alcohol were mixed and 4.6 grams of sodium wire (2.0 mols.) added. After heating for three hours reaction had ceased and a white precipitate had deposited in the bottom of the flask. The product was cooled to room temperature and the ethyl benzoate was poured in. The remaining wire gradually became yellow and then brown. At the end of an hour the solution was yellow and a heavy white precipitate was observed in the bottom of the flask. The coil of wire was brown. After boiling during two days the metal had all disappeared. A second atomic proportion of sodium was now added and the heating continued for two days longer. This caused almost all of the wire to react. A third atomic proportion of sodium was placed in the flask and the heating prolonged during several days, but no further appreciable reaction took place. The solution was now a reddish brown, with a bulky precipitate which, as seen through the solution, appeared to be yellow in color. The camphor, dissolved in some ligroin and ether, was now added to the product of the reaction and the heating continued for four hours. The "solvent product" was a yellow oil. The "acidification product" consisted of 5.6 grams of benzoic acid and 1.4 grams of crude diketone. The quantity of the acid is equal to 7.2 grams of the ester.

Experiment 62.—15.0 grams ethyl benzoate (1 mol.); 4.6 grams sodium wire (2 atoms); 200 cc. petroleum ether (b. p. 36°).

The ester, solvent, and half of the sodium were heated during eight hours, at the end of which time the metal had disappeared. The remainder of the sodium was then added, and the heating continued for ten hours longer. This portion of

the wire also dissolved, but there was no reaction when a third atomic proportion of the metal was added and the heating prolonged for another ten hours. The "solvent product" consisted of 0.7 gram of a yellow, amorphous solid. The "acidification product" contained 5.4 grams of benzoic acid, in addition to an amorphous substance from which no crystalline derivative could be obtained by the action of benzoyl chloride (cf. Exp. 66). Allowing for the unavoidable loss in the separation and purification, the above quantity of benzoic acid is equal to one-half of the ester used, the exact ratio being 6 grams of acid: 7.5 grams of ester.

Experiment 63.—7.5 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (2 atoms); 250 cc. ether.

The reaction commenced immediately and at the end of an hour a brown precipitate began to form. The heating was continued during three days, two additional atomic proportions of sodium being added, but these apparently were not attacked. The "solvent product" consisted of 0.5 gram of a yellow oil, containing some white crystals. The "acidification product" yielded 3.9 grams of benzoic acid, equivalent to 5 grams of the acid. Speaking generally, this experiment presented the same features as those in which camphor and ethyl benzoate were condensed.

Experiment 64.—7.5 grams ethyl benzoate (1 mol.); sodium hydroxide (4 mols.); 250 cc. ether.

The hydroxide was equivalent to the total quantity of sodium used in the preceding experiment. It was dissolved in ice water and shaken with the ester, dissolved in the ether. The time occupied in the manipulation and the other conditions were exactly the same as those in Exp. 63. The "solvent product" consisted of 7.1 grams of ethyl benzoate, and the "acidification product," when dissolved in ether and treated with aqueous sodium bicarbonate, yielded 0.1 gram of benzoic acid, equivalent to 0.123 gram of the ester, thus leaving only 0.277 gram of the ester unaccounted for. This result shows that practically none of the benzoic acid which separated in the experiments described above can be formed as a

result of the hydrolysis of ethyl benzoate during the extraction processes.

Experiment 65.—The "solvent products" from five different experiments with ethyl benzoate and camphor, under varied conditions, which had given very poor relative yields of diketone, were combined and distilled with steam. The volatile material was separated from the water, dried, and filtered. The solid consisted of 20 grams of a mixture of camphor and borneol. The liquid portion, after being fractionated, yielded 40 grams of benzyl alcohol, which is equivalent to about half of the ethyl benzoate employed.

Experiment 66.—3.75 grams ethyl benzoate (1 mol.); 1.15 grams sodium wire (2 atoms); 200 cc. ether.

The solid product of the reaction, which was carried out in the manner described under Exp. 63, was filtered quickly, washed several times with ether, in a closed flask, and the red solid obtained suspended in ether. Excess of *m*-nitrobenzoyl chloride and aqueous alkali were now added and the mixture shaken thoroughly. A compound deposited gradually as yellow crystals, which, after purification, melted above 310° . This substance was dissolved in 50 per cent alcohol, excess of aqueous sodium hydroxide added, and the liquid allowed to remain at the room temperature during two days. When acid was added to the solution a heavy, white precipitate was formed. This melted at 141° to 142° and was, therefore, identified as being *m*-nitrobenzoic acid. No benzoin was isolated, but the yellow compound of high melting point described above was prepared synthetically from *m*-nitrobenzoyl chloride and benzoin, in the presence of an alkali.

The results described above confirm the conclusion that, in addition to sodium ethylate, sodium and benzoic ester

yield the compound $\text{C}_6\text{H}_5\text{CONa}$
 $\text{C}_6\text{H}_5\text{CONa}$ $\parallel$, which, with water, gives

sodium benzoate and benzyl alcohol, in equimolecular proportions. Under suitable conditions, however, the hypo-

thetical hydrolysis product, $\text{C}_6\text{H}_5\text{COH}$
 $\text{C}_6\text{H}_5\text{COH}$ $\parallel$, changes into benzoin,

$\text{C}_6\text{H}_5\text{CH}(\text{OH})\text{COC}_6\text{H}_5$, which was isolated in the form of its *m*-nitrobenzoyl compound.

The results also demonstrate that this reaction between the metal and the ester is by far the preponderant one under all the rather varied experimental conditions which have been employed.

BIOGRAPHICAL.

Ernest E. Gorsline was born near Rochester, N. Y., May 27, 1877. He was educated in the public schools of Rochester and graduated from the Rochester Free Academy in 1895. Two years later he entered the University of Rochester and graduated in 1901 with the degree of B.S. He was teacher of chemistry and physics in Peddie Institute during the next two years and in the following year was laboratory assistant in Brooklyn Girls' High School. In 1904 he entered the Johns Hopkins University as a graduate student and was appointed assistant in chemistry at the University of Rochester in 1906.

